Claims

1. An isolated nucleic acid molecule selected from the group consisting of

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:1, and which code for a murine TLR9 having an amino acid sequence set forth as SEQ ID NO:3,

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to degeneracy of the genetic code, and

(c) complements of (a) or (b).

2. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule codes for SEQ ID NO:3.

3. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO:1.

4. The isolated nucleic acid molecule of claim 1, wherein the isolated nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:2.

5. An isolated TLR9 polypeptide or fragment thereof comprising at least one amino acid of murine TLR9 selected from the group consisting of amino acids 2, 3, 4, 6, 7, 18, 19, 22, 38, 44, 55, 58, 61, 62, 63, 65, 67, 71, 80, 84, 87, 88, 91, 101, 106, 109, 117, 122, 123, 134, 136, 140, 143, 146, 147, 157, 160, 161, 167, 168, 171, 185, 186, 188, 189, 191, 199, 213, 217, 220, 227, 231, 236, 245, 266, 269, 270, 271, 272, 273, 274, 278, 281, 285, 297, 298, 301, 305, 308, 311, 322, 323, 325, 326, 328, 332, 335, 346, 348, 353, 355, 358, 361, 362, 365, 367, 370, 372, 380, 381, 382, 386, 389, 392, 394, 397, 409, 412, 413, 415, 416, 419, 430, 432, 434, 435, 438, 439, 443, 444, 446, 447, 448, 450, 451, 452, 454, 455, 459, 460, 463, 465, 466, 468, 469, 470, 472, 473, 474, 475, 478, 488, 489, 494, 495, 498, 503, 508, 510, 523, 531, 539, 540, 543, 547, 549, 561, 563, 565, 576, 577, 579, 580, 587, 590, 591, 594, 595, 597, 599, 601, 603, 610, 611, 613, 616, 619, 632, 633, 640, 643, 645, 648, 650, 657, 658, 660, 667, 670, 672, 675, 679, 689, 697, 700, 703, 705, 706, 711, 715, 716, 718, 720, 723, 724, 726, 729, 731, 735, 737, 743, 749, 750, 751, 752, 754, 755, 759, 760,

772, 774, 780, 781, 786, 787, 788, 800, 814, 821, 829, 831, 832, 835, 844, 857, 858, 859, 862, 864, 865, 866, 879, 893, 894, 898, 902, 910, 917, and 927 of SEQ ID NO:3, wherein the TLR9 polypeptide or fragment thereof has an amino acid sequence which is identical to a human TLR9 polypeptide or fragment thereof except for the at least one amino acid of murine TLR9.

6. The isolated TLR9 polypeptide or fragment thereof of claim 5, further comprising at least one amino acid of murine TLR9 selected from the group consisting of amino acids 949, 972, 975, 976, 994, 997, 1000, 1003, 1004, 1010, 1011, 1018, 1023, and 1027 of SEQ ID NO:3.

7. The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the human TLR9 has an amino acid sequence set forth as SEQ ID NO:6.

8. The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof has an amino acid sequence selected from the group consisting of SEQ ID NO:3 and fragments of SEQ ID NO:3.

9. The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof is an extracytoplasmic domain of TLR9.

10. The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof comprises an MBD motif as set forth as SEQ ID NO:126 or SEQ ID NO:127.

11. The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof selectively binds to an immunostimulatory nucleic acid (ISNA).

12. The isolated TLR9 polypeptide or fragment thereof of claim 5, wherein the isolated TLR9 polypeptide or fragment thereof selectively binds to a CpG nucleic acid.

13. An isolated nucleic acid molecule which encodes the isolated TLR9 polypeptide or fragment thereof of claim 5.

14. An expression vector comprising the isolated nucleic acid molecule of claim 1 operably linked to a promoter.

15. A host cell comprising the expression vector of claim 14.

16. The host cell of claim 15, further comprising at least one expression vector selected from the group consisting of:

(a) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR7 polypeptide operably linked to a promoter, and

(b) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR8 polypeptide operably linked to a promoter.

17. The host cell of claim 15, further comprising a reporter construct capable of interacting with a TIR domain.

18. An expression vector comprising the isolated nucleic acid molecule of claim 13 operably linked to a promoter.

19. A host cell comprising the expression vector of claim 18.

20. The host cell of claim 19, further comprising at least one expression vector selected from the group consisting of:

(a) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR7 polypeptide operably linked to a promoter, and

(b) an expression vector comprising a nucleic acid molecule which encodes an isolated TLR8 polypeptide operably linked to a promoter.

21. The host cell of claim 19, further comprising a reporter construct capable of interacting with a TIR domain.

22. An isolated nucleic acid molecule selected from the group consisting of

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:173, and which code for a murine TLR7 having an amino acid sequence set forth as SEQ ID NO:175,

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to degeneracy of the genetic code, and

(c) complements of (a) or (b).

23. The isolated nucleic acid molecule of claim 22, wherein the isolated nucleic acid molecule codes for SEQ ID NO:175.

24. The isolated nucleic acid molecule of claim 22, wherein the isolated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO:173.

25. The isolated nucleic acid molecule of claim 22, wherein the isolated nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:174.

26. An isolated TLR7 polypeptide or fragment thereof comprising at least one amino acid of murine TLR7 selected from the group consisting of amino acids 4, 8, 15, 16, 18, 21, 23, 24, 25, 27, 37, 39, 40, 41, 42, 44, 45, 61, 79, 83, 86, 89, 92, 96, 103, 109, 111, 113, 119, 121, 127, 128, 131, 145, 148, 151, 164, 172, 176, 190, 202, 203, 204, 205, 222, 225, 226, 228, 236, 238, 243, 250, 253, 266, 268, 271, 274, 282, 283, 287, 288, 308, 313, 314, 315, 325, 328, 331, 332, 341, 343, 344, 347, 351, 357, 360, 361, 362, 363, 364, 365, 366, 370, 371, 377, 378, 387, 388, 389, 392, 397, 398, 413, 415, 416, 419, 421, 422, 425, 437, 438, 440, 446, 449, 453, 454, 455, 456, 462, 470, 482, 486, 487, 488, 490, 491, 493, 494, 503, 505, 509, 511, 529, 531, 539, 540, 543, 559, 567, 568, 574, 583, 595, 597, 598, 600, 611, 613, 620, 624, 638, 645, 646, 651, 652, 655, 660, 664, 665, 668, 669, 672, 692, 694, 695, 698, 701, 704, 714, 720, 724, 727, 728, 733, 738, 745, 748, 755, 762, 777, 780, 789,

803, 846, 850, 851, 860, 864, 868, 873, 875, 884, 886, 888, 889, 890, 902, 903, 911, 960, 967, 970, 980, 996, 1010, 1018, 1035, and 1045 of SEQ ID NO:175, wherein the TLR7 polypeptide or fragment thereof has an amino acid sequence which is identical to a human TLR7 polypeptide or fragment thereof except for the at least one amino acid of murine TLR7.

27. The isolated TLR7 polypeptide or fragment thereof of claim 26, wherein the human TLR7 has an amino acid sequence set forth as SEQ ID NO:170.

28. The isolated TLR7 polypeptide or fragment thereof of claim 26, wherein the isolated TLR7 polypeptide or fragment thereof has an amino acid sequence selected from the group consisting of SEQ ID NO:175 and fragments of SEQ ID NO:175.

29. The isolated TLR7 polypeptide or fragment thereof of claim 26, wherein the isolated TLR7 polypeptide or fragment thereof is an extracytoplasmic domain of TLR7.

30. The isolated TLR7 polypeptide or fragment thereof of claim 26, wherein the isolated TLR7 polypeptide or fragment thereof comprises an MBD motif as set forth as any one of SEQ ID NOs: 203, 204, 212, and 213.

31. The isolated TLR7 polypeptide or fragment thereof of claim 26, wherein the isolated TLR7 polypeptide or fragment thereof selectively binds to an ISNA.

32. The isolated TLR7 polypeptide or fragment thereof of claim 26, wherein the isolated TLR7 polypeptide or fragment thereof selectively binds to a CpG nucleic acid.

33. An isolated nucleic acid molecule which encodes the isolated TLR7 polypeptide or fragment thereof of claim 26.

34. An expression vector comprising the isolated nucleic acid molecule of claim 22 operably linked to a promoter.

35. A host cell comprising the expression vector of claim 34.

36. The host cell of claim 35, further comprising a reporter construct capable of interacting with a TIR domain.

37. An expression vector comprising the isolated nucleic acid molecule of claim 33 operably linked to a promoter.

38. A host cell comprising the expression vector of claim 37.

39. The host cell of claim 38, further comprising a reporter construct capable of interacting with a TIR domain.

40. An isolated nucleic acid molecule selected from the group consisting of

(a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:190, and which code for a murine TLR8 having an amino acid sequence set forth as SEQ ID NO:192,

(b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to degeneracy of the genetic code, and

(c) complements of (a) or (b).

41. The isolated nucleic acid molecule of claim 40, wherein the isolated nucleic acid molecule codes for SEQ ID NO:192.

42. The isolated nucleic acid molecule of claim 40, wherein the isolated nucleic acid molecule comprises the nucleotide sequence set forth as SEQ ID NO:190.

43. The isolated nucleic acid molecule of claim 40, wherein the isolated nucleic acid molecule comprises a nucleotide sequence set forth as SEQ ID NO:191.

44. An isolated TLR8 polypeptide or fragment thereof comprising at least one amino acid of murine TLR8 selected from the group consisting of amino acids 5, 6, 9, 10, 14, 15, 18, 21, 22, 23, 24, 25, 26, 27, 28, 30, 39, 40, 41, 43, 44, 50, 51, 53, 55, 61, 67, 68, 74, 80, 85, 93, 98, 99, 100, 104, 105, 106, 107, 110, 114, 117, 119, 121, 124, 125, 134, 135, 138, 145, 155, 156, 157, 160, 161, 162, 163, 164, 166, 169, 170, 174, 180, 182, 183, 186, 187, 191, 193, 194, 196, 197, 199, 200, 207, 209, 210, 227, 228, 230, 231, 233, 234, 241, 256, 263, 266, 267, 268, 269, 272, 274, 275, 276, 280, 285, 296, 298, 299, 300, 303, 305, 306, 307, 310, 312, 320, 330, 333, 335, 343, 344, 345, 346, 347, 349, 351, 356, 362, 365, 366, 375, 378, 379, 380, 381, 383, 384, 386, 387, 392, 402, 403, 408, 414, 416, 417, 422, 426, 427, 428, 429, 430, 431, 433, 437, 438, 439, 440, 441, 444, 445, 449, 456, 461, 463, 471, 483, 486, 489, 490, 494, 495, 496, 505, 507, 509, 512, 513, 519, 520, 523, 537, 538, 539, 541, 542, 543, 545, 554, 556, 560, 567, 569, 574, 575, 578, 586, 592, 593, 594, 595, 597, 599, 602, 613, 617, 618, 620, 621, 623, 628, 630, 633, 639, 641, 643, 644, 648, 655, 658, 661, 663, 664, 666, 668, 677, 680, 682, 687, 688, 690, 692, 695, 696, 697, 700, 702, 703, 706, 714, 715, 726, 727, 728, 730, 736, 738, 739, 741, 746, 748, 751, 752, 754, 757, 764, 766, 772, 776, 778, 781, 784, 785, 788, 791, 795, 796, 801, 802, 806, 809, 817, 820, 821, 825, 828, 829, 831, 839, 852, 853, 855, 858, 863, 864, 900, 903, 911, 918, 934, 977, 997, 1003, 1008, 1010, 1022, 1023, 1024, 1026, and 1030 of SEQ ID NO:192, wherein the TLR8 polypeptide or fragment thereof has an amino acid sequence which is identical to a human TLR8 polypeptide or fragment thereof except for the at least one amino acid of murine TLR8.

45. The isolated TLR8 polypeptide or fragment thereof of claim 44, wherein the human TLR8 has an amino acid sequence set forth as SEQ ID NO:184.

46. The isolated TLR8 polypeptide or fragment thereof of claim 44, wherein the isolated TLR8 polypeptide or fragment thereof has an amino acid sequence selected from the group consisting of SEQ ID NO:192 and fragments of SEQ ID NO:192.

47. The isolated TLR8 polypeptide or fragment thereof of claim 44, wherein the isolated TLR8 polypeptide or fragment thereof is an extracytoplasmic domain of TLR8.

48. The isolated TLR8 polypeptide or fragment thereof of claim 44, wherein the isolated TLR8 polypeptide or fragment thereof comprises an MBD motif as set forth as any one of SEQ ID NOs: 205, 206, 214, and 215.

49. The isolated TLR8 polypeptide or fragment thereof of claim 44, wherein the isolated TLR8 polypeptide or fragment thereof selectively binds to an ISNA.

50. The isolated TLR8 polypeptide or fragment thereof of claim 44, wherein the isolated TLR8 polypeptide or fragment thereof selectively binds to a CpG nucleic acid.

51. An isolated nucleic acid molecule which encodes the isolated TLR8 polypeptide or fragment thereof of claim 44.

52. An expression vector comprising the isolated nucleic acid molecule of claim 40 operably linked to a promoter.

53. A host cell comprising the expression vector of claim 52.

54. The host cell of claim 53, further comprising a reporter construct capable of interacting with a TIR domain.

55. An expression vector comprising the isolated nucleic acid molecule of claim 51 operably linked to a promoter.

56. A host cell comprising the expression vector of claim 55.

57. The host cell of claim 56, further comprising a reporter construct capable of interacting with a TIR domain.

58. An isolated nucleic acid molecule which hybridizes under stringent conditions to the

isolated nucleic acid molecule of claim 1 or claim 13.

59. A method for inhibiting TLR9 signaling activity in a cell, comprising:

contacting the cell with an isolated nucleic acid molecule of claim 58 in an amount effective to inhibit expression of TLR9 polypeptide in the cell.

60. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the nucleotide sequence of the isolated nucleic acid molecule of claim 1 or claim 13.

61. A method for inhibiting TLR9 signaling activity in a cell, comprising:

contacting the cell with an isolated nucleic acid molecule of claim 60 in an amount effective to inhibit expression of TLR9 polypeptide in the cell.

62. A method for identifying nucleic acid molecules which interact with a TLR polypeptide or a fragment thereof, comprising:

contacting a TLR polypeptide selected from the group consisting of TLR7, TLR8, TLR9, and nucleic acid-binding fragments thereof with a test nucleic acid molecule; and

measuring an interaction of the test nucleic acid molecule with the TLR polypeptide or fragment thereof.

63. The method of claim 62, wherein the TLR polypeptide or fragment thereof is expressed in a cell.

64. The method of claim 62, wherein the TLR polypeptide or fragment thereof is an isolated TLR polypeptide or fragment thereof.

65. The method of claim 64, wherein the isolated TLR polypeptide or fragment thereof is immobilized on a solid support.

66. The method of claim 62, wherein the TLR polypeptide or fragment thereof is fused

with an Fc fragment of an antibody.

67. The method of claim 66, wherein the TLR polypeptide or fragment thereof comprises a TLR extracytoplasmic domain.

68. The method of claim 62, wherein the interaction is binding.

69. The method of claim 68, wherein the measuring is accomplished by a method selected from the group consisting of enzyme-linked imunosorbent assay (ELISA), biomolecular interaction assay (BIA), electromobility shift assay (EMSA), radioimmunoassay (RIA), polyacrylamide gel electrophoresis (PAGE), and Western blotting.

70. The method of claim 63, wherein the measuring is accomplished by a method comprising measuring a response mediated by a TLR signal transduction pathway.

71. The method of claim 70, wherein the response mediated by a TLR signal transduction pathway is selected from the group consisting of induction of a gene under control of NF-κB promoter and secretion of a cytokine.

72. The method of claim 71, wherein the gene under control of NF-κB promoter is selected from the group consisting of IL-8, IL-12 p40, NF-κB-luc, IL-12 p40-luc, and TNF-luc.

73. The method of claim 71, wherein the cytokine is selected from the group consisting of IL-8, TNF-α, and IL-12 p40.

74. The method of claim 70, further comprising:

comparing (a) the response mediated by a TLR signal transduction pathway as measured in presence of the test nucleic acid molecule with (b) a response mediated by a TLR signal transduction pathway as measured in absence of the test nucleic acid molecule; and

determining the test nucleic acid molecule is an ISNA when (a) exceeds (b).

75. The method of claim 70, further comprising:

comparing the response to a reference response when the TLR polypeptide is independently contacted with a reference nucleic acid molecule; and

determining if the response is stronger or weaker than the reference response.

76. The method of claim 70, further comprising:

comparing the response to a reference response when the TLR polypeptide is concurrently contacted with a reference nucleic acid molecule; and

determining if the response is stronger or weaker than the reference response.

77. The method of claim 62, wherein the TLR polypeptide or fragment thereof is TLR7.

78. The method of claim 62, wherein the TLR polypeptide or fragment thereof is TLR8.

79. The method of claim 62, wherein the TLR polypeptide or fragment thereof is TLR9.

80. A screening method for identifying an ISNA, comprising:

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 with a test nucleic acid molecule;

detecting presence or absence of a response mediated by a TLR signal transduction pathway in the presence of the test nucleic acid molecule arising as a result of an interaction between the functional TLR and the test nucleic acid molecule; and

determining the test nucleic acid molecule is an ISNA when the presence of a response mediated by the TLR signal transduction pathway is detected.

81. The method of claim 80, further comprising comparing the response mediated by the TLR signal transduction pathway arising as a result of an interaction between the functional TLR and the test nucleic acid molecule with a response arising as a result of an interaction between the functional TLR and a reference ISNA.

82. The method of claim 81, wherein the screening method is performed on a plurality of test nucleic acid molecules.

83. The method of claim 82, wherein the response mediated by the TLR signal transduction pathway is measured quantitatively and wherein the response mediated by the TLR signal transduction pathway associated with each of the plurality of test nucleic acid molecules is compared with a response arising as a result of an interaction between the functional TLR and a reference ISNA.

84. The method of claim 83, wherein a subset of the plurality of test nucleic acid molecules is selected based on ability of the subset to produce a specific response mediated by the TLR signal transduction pathway.

85. The method of claim 80, wherein the functional TLR is expressed in a cell.

86. The method of claim 85, wherein the cell is an isolated mammalian cell that naturally expresses the functional TLR.

87. The method of claim 86, wherein the cell comprises an expression vector comprising an isolated nucleic acid which encodes a reporter construct selected from the group consisting of IL-8, IL-12 p40, NF-κB-luc, IL-12 p40-luc, and TNF-luc.

88. The method of claim 80, wherein the functional TLR is part of a cell-free system.

89. The method of claim 80, wherein the functional TLR is part of a complex with another TLR.

90. The method of claim 89, wherein the complex is a complex of TLR9 and TLR7.

91. The method of claim 89, wherein the complex is a complex of TLR9 and TLR8.

92. The method of claim 80, wherein the functional TLR is part of a complex with a non-TLR protein selected from the group consisting of MyD88, IRAK, TRAF6, IκB, NF-κB, and functional homologues and derivatives thereof.

93. The method of claim 80, wherein the reference ISNA is a CpG nucleic acid.

94. The method of claim 80, wherein the test nucleic acid molecule is a CpG nucleic acid.

95. The method of claim 80, wherein the response mediated by a TLR signal transduction pathway is selected from the group consisting of induction of a gene under control of NF-κB promoter and secretion of a cytokine.

96. The method of claim 95, wherein the gene under control of NF-κB promoter is selected from the group consisting of IL-8, IL-12 p40, NF-κB-luc, IL-12 p40-luc, and TNF-luc.

97. The method of claim 95, wherein the cytokine is selected from the group consisting of IL-8, TNF-α, and IL-12 p40.

98. A screening method for comparing TLR signaling activity of a test compound with an ISNA, comprising:

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 with a reference ISNA and detecting a reference response mediated by a TLR signal transduction pathway;

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 with a test compound and detecting a test response mediated by a TLR signal transduction pathway; and

comparing the test response with the reference response to compare the TLR signaling activity of the test compound with the ISNA.

99. The method of claim 98, wherein the functional TLR is contacted with the reference ISNA and the test compound independently.

100. The method of claim 99, wherein the screening method is a method for identifying an ISNA mimic, and wherein when the test response is similar to the reference response the test compound is an ISNA mimic.

101. The method of claim 98, wherein the functional TLR is contacted with the reference ISNA and the test compound concurrently to produce a test-reference response mediated by a TLR signal transduction pathway and wherein the test-reference response may be compared to the reference response.

102. The method of claim 101, wherein the screening method is a method for identifying an ISNA agonist, and wherein when the test-reference response is greater than the reference response the test compound is an ISNA agonist.

103. The method of claim 101, wherein the screening method is a method for identifying an ISNA antagonist, and wherein when the test-reference response is less than the reference response the test compound is an ISNA antagonist.

104. The method of claim 98, wherein the functional TLR is expressed in a cell.

105. The method of claim 104, wherein the cell is an isolated mammalian cell that naturally expresses the functional TLR9.

106. The method of claim 105, wherein the cell comprises an expression vector comprising an isolated nucleic acid which encodes a reporter construct selected from the group consisting of IL-8, IL-12 p40, NF-κB-luc, IL-12 p40-luc, and TNF-luc.

107. The method of claim 98, wherein the functional TLR is part of a cell-free system.

108. The method of claim 98, wherein the functional TLR is part of a complex with another TLR.

109. The method of claim 98, wherein the functional TLR is part of a complex with a non-TLR protein selected from the group consisting of MyD88, IRAK, TRAF6, IκB, NF-κB, and functional homologues and derivatives thereof.

110. The method of claim 98, wherein the reference ISNA is a CpG nucleic acid.

111. The method of claim 98, wherein the test compound is not a nucleic acid molecule.

112. The method of claim 98, wherein the test compound is a polypeptide.

113. The method of claim 98, wherein the test compound is a part of a combinatorial library of compounds.

114. A screening method for identifying species specificity of an ISNA, comprising:

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 of a first species with a test ISNA;

contacting a functional TLR selected from the group consisting of TLR7, TLR8, and TLR9 of a second species with the test ISNA;

measuring a response mediated by a TLR signal transduction pathway associated with the contacting the functional TLR of the first species with the test ISNA;

measuring a response mediated by the TLR signal transduction pathway associated with the contacting the functional TLR of the second species with the test ISNA; and

comparing (a) the response mediated by a TLR signal transduction pathway associated with the contacting the functional TLR of the first species with the test ISNA with (b) the response mediated by the TLR signal transduction pathway associated with the contacting the functional TLR of the second species with the test ISNA.

115. The method of claim 114, wherein the functional TLR is expressed in a cell.

116. The method of claim 115, wherein the cell is an isolated mammalian cell that naturally expresses the functional TLR.

117. The method of claim 114, wherein the functional TLR is part of a cell-free system.

118. The method of claim 114, wherein the functional TLR is part of a complex with another TLR.

119. The method of claim 114, wherein the functional TLR is part of a complex with a non-TLR protein selected from the group consisting of MyD88, IRAK, TRAF6, IκB, NF-κB, and functional homologues and derivatives thereof.

120. A method for identifying lead compounds for a pharmacological agent useful in treatment of disease associated with TLR9 signaling activity, comprising

providing a cell comprising a TLR9 as provided in claim 5;

contacting the cell with a candidate pharmacological agent under conditions which, in the absence of the candidate pharmacological agent, cause a first amount of TLR9 signaling activity; and

determining a second amount of TLR9 signaling activity as a measure of the effect of the pharmacological agent on the TLR9 signaling activity, wherein a second amount of TLR9 signaling activity which is less than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which reduces TLR9 signaling activity and wherein a second amount of TLR9 signaling activity which is greater than the first amount indicates that the candidate pharmacological agent is a lead compound for a pharmacological agent which increases TLR9 signaling activity.